



2-20-07

1626

Attorney's Docket No.: 20750-038US1 / 029.US2.PCT

## IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant : Graeme Semple, et al.                      Art Unit : 1626  
Serial No. : 10/530,902                                      Examiner : Rebecca L. Anderson  
Filed : April 8, 2005                                        Conf. No. : 2895  
Title : 5-SUBSTITUTED 2H-PYRAZONE-3-CARBOXYLIC ACID DERIVATIVES AS  
ANTILIPOLYTIC AGENTS FOR THE TREATMENT OF METABOLIC-  
RELATED DISORDERS SUCH AS DYSLIPIDEMIA

**MAIL STOP AMENDMENT**

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Applicants request consideration of the references listed on the attached PTO-1449 form. Under 37 C.F.R. § 1.98 (a)(2)(ii), only copies of foreign patent documents and/or non-patent literature are enclosed. Copies of any listed U.S. patents or U.S. patent application publications can be provided upon request. A copy of a communication from a foreign patent office in a counterpart application is also enclosed.

This statement is being filed within three months of the filing date of the application or before the receipt of a first Office Action on the merits. Please apply any charges or credits to Deposit Account No. 06-1050.

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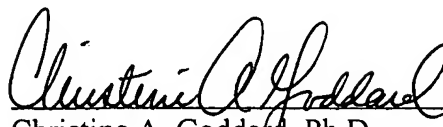
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Serial No. : 10/530,902  
Filed : April 8, 2005  
Page : 2 of 2

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Respectfully submitted,

Date: February 15, 2007

  
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**INFORMATION DISCLOSURE  
STATEMENT BY APPLICANT**

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Sheet 1 of 6

**Complete if Known**

|                        |                     |
|------------------------|---------------------|
| Application Number     | 10/530,902          |
| Filing Date            | April 8, 2005       |
| First Named Inventor   | Graeme Semple       |
| Art Unit               | 1626                |
| Examiner Name          | Anderson, Rebecca L |
| Attorney Docket Number | 29.US2.PCT          |

**U.S. PATENT DOCUMENTS**

| Examiner<br>Initials * | Cite<br>No. <sup>1</sup> | Document Number                            | Publication/Issue Date<br>MM-DD-YYYY | Name of Patentee or Applicant of<br>Cited Document | Pages, Columns, Lines, Where Relevant<br>Passages or Relevant<br>Figures Appear |
|------------------------|--------------------------|--|--------------------------------------|--|---|
|                        |                          | Number - Kind Code <sup>2</sup> (if known) |                                      |  |   |
|                        | FL                       | US-2005/154024                             | 07-14-2005                           | Bryans <i>et al.</i> ,                             |   |
|                        | FM                       | US-2005/182108                             | 08-18-2005                           | Carson <i>et al.</i> ,                             |   |
|                        | FN                       | US-6,444,816 B1                            | 09-03-2002                           | Das <i>et al.</i> ,                                |   |

**FOREIGN PATENT DOCUMENTS**

| Examiner<br>Initials * | Cite<br>No. <sup>1</sup> | Foreign Patent Document   | Publication<br>Date/Filing Date<br>MM-DD-YYYY | Name of Patentee or Applicant<br>of Cited Document | Pages,<br>Columns, Lines,<br>Where Relevant<br>Passages or<br>Relevant<br>Figures Appear | T <sup>6</sup> |
|------------------------|--------------------------|---|---|--|--|----------------|
|                        |                          | Country Code <sup>3</sup> - Number <sup>4</sup> - Kind Code <sup>5</sup> (if known) |   |  |  |                |
|                        | FO                       | WO2003/032928 A1  | 04-22-2004                                    | Arena Pharmaceuticals, Inc.                        |  |                |
|                        | FP                       | WO2004/054974   | 07-01-2004                                    | SmithKline Beecham<br>Corporation                  |  |                |
|                        | FQ                       | WO2005/009965   | 02-03-2005                                    | Pfizer Ltd.  |  |                |
|                        | FR                       | WO2005/084663   | 09-15-2005                                    | Janssen Pharmaceutica                              |  |                |
|                        | FS                       | WO2006/023750   | 03-02-2006                                    | Merck & Co., Inc.                                  |  |                |
|                        | FT                       | WO2006/032519   | 03-30-2006                                    | Hoffmann-La Roche                                  |  |                |
|                        | FU                       | WO2006/032851   | 03-30-2006                                    | Bioliopox AB                                       |  |                |
|                        | FV                       | WO2006/032852   | 03-30-2006                                    | Bioliopox AB                                       |  |                |
|                        | FW                       | WO2006/052569   | 05-18-2006                                    | Arena Pharmaceuticals, Inc.                        |  |                |
|                        | FX                       | WO02/22601  | 03-21-2002                                    | Vertex Pharmaceuticals,<br>Inc.                    |  |                |
|                        | FY                       | WO00/69849  | 11-23-2000                                    | Ortho-McNeil<br>Pharmaceutical, Inc.               |  |                |
|                        | FZ                       | WO03/099793   | 12-04-2003                                    | Takeda Chemical<br>Industries, Ltd.                |  |                |
|                        | GA                       | WO2004/033431   | 04-22-2004                                    | Arena Pharmaceuticals, Inc.                        |  |                |
|                        | GB                       | GB 1048104  | 11-09-1966                                    | The Upjohn Company                                 |  |                |
|                        | GC                       | JP 54014968   | 02-03-1979                                    | Taiho Pharmaceutical Co.<br>Ltd.                   |  |                |
|                        | GD                       | HU184940B   | 11-28-1984                                    | Gyogyszerkutato Intezet                            |  |                |

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| Examiner<br>Initials * | Cite<br>No. <sup>1</sup> | Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.   | T <sup>2</sup> |
|------------------------|--------------------------|---|----------------|
|                        | GE                       | FROESCH <i>et al.</i> , Effects of 5-methylpyrazole-3-carboxylic acid on adipose tissue. I. Inhibition of lipolysis, effects on glucose, fructose, and glycogen metabolism in vitro and comparison with insulin. <i>Molecular Pharmacol.</i> (1967), 3(5), 429-41 |                |
|                        | GF                       | MUGNAINI <i>et al.</i> Heterocyclic syntheses with propargyl alcohol and butynediol. II. <i>Classe sci. fis., mat. e nat.</i> (1953), 14, 275-80  |                |
|                        | GG                       | MUGNAINI <i>et al.</i> Heterocyclic syntheses with propargyl alcohol and butynediol. <i>Classe sci. fis., mat. e nat.</i> (1953), 14, 95-8  |                |
|                        | GH                       | HÜTTEL Über einige Aldehyde der Pyrazol- und der 1.2.3-Triazol-Reihe. <i>Berichte der deutschen chemischen Gesellschaft (A and B Series)</i> 74(10), 1941, 1680-1687  |                |
|                        | GI                       | PANIZZI <i>et al.</i> Heterocyclic syntheses. VII. Some pyrazolic ketones. <i>Gazzetta Chimica Italiana</i> (1946), 76, 66-77   |                |
|                        | GJ                       | MELANI <i>et al.</i> Synthesis of 5H-10,11-dihydropyrazolo[5,1-c][1,4]benzodiazepine derivatives. II. <i>Journal of Heterocyclic Chemistry</i> (1984), 21(3), 813-15  |                |
|                        | GK                       | KLAGES <i>et al.</i> Pyrazoles from 1:3-diketones and alkyl diazoacetates. <i>Journal fuer Praktische Chemie</i> (1902), 65(ii), 387-93   |                |
|                        | GL                       | OWEN <i>et al.</i> Olefinic acids. II. Reactivity of $\alpha$ -bromoacrylic acid and some related compounds. <i>Journal of the Chemical Society</i> (1947), 1030-4  |                |
|                        | GM                       | ABDALLAH <i>et al.</i> Diazoacetaldehyde dimethyl acetal: a new route to cyclopropane aldehydes and formylpyrazoles. <i>Tetrahedron Letters</i> (1980), 21(23), 2239-42   |                |
|                        | GN                       | International Search Report, WO 2005/011677, 12/10/2004   |                |
|                        | GO                       | ALTSCHUL <i>et al.</i> Influence of nicotinic acid on serum cholesterol in man. <i>Archives of biochemistry</i> (1955), 54(2), 558-9  |                |
|                        | GP                       | TAVINTHARAN <i>et al.</i> The benefits of niacin in atherosclerosis. <i>Current atherosclerosis reports</i> (2001), 3(1), 74-82   |                |
|                        | GQ                       | CARLSON <i>et al.</i> Nicotinic acid: the broad-spectrum lipid drug. A 50th anniversary review. <i>Journal of Internal Medicine</i> (2005), 258(2), 94-114  |                |

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Date  
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Sheet 3 of 6

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| First Named Inventor   | Graeme Semple       |
| Art Unit               | 1626                |
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|---------------------|-----------------------|---|----------------|
|                     | GR                    | LORENZEN <i>et al.</i> Characterization of a G protein-coupled receptor for nicotinic acid. <i>Molecular Pharmacology</i> (2001), 59(2), 349-357  |                |
|                     | GS                    | SOGA <i>et al.</i> Molecular identification of nicotinic acid receptor. <i>Biochemical and Biophysical Research Communications</i> (2003), 303(1), 364-369  |                |
|                     | GT                    | TUNARU <i>et al.</i> PUMA-G and HM74 are receptors for nicotinic acid and mediate its anti-lipolytic effect. <i>Nature Medicine</i> (2003), 9(3), 352-355   |                |
|                     | GU                    | ZHANG <i>et al.</i> , Niacin mediates lipolysis in adipose tissue through its G-protein coupled receptor HM74A. <i>Biochemical and Biophysical Research Communications</i> (2005), 334(2), 729-732  |                |
|                     | GV                    | BENYO <i>et al.</i> GPR109A (PUMA-G/HM74A) mediates nicotinic acid-induced flushing. <i>Journal of Clinical Investigation</i> (2005), 115(12), 3634-3640  |                |
|                     | GW                    | O'KANE <i>et al.</i> A comparison of acipimox and nicotinic acid in type 2b hyperlipidaemia. <i>British journal of clinical pharmacology</i> (1992), 33(4), 451-3   |                |
|                     | GX                    | JIRKOVSKY <i>et al.</i> , Hypolipidemic 4,5-dihydro-4-oxo-5,5-disubstituted-2-furancarboxylic acids. <i>Journal of Medicinal Chemistry</i> (1982), 25(10), 1154-6   |                |
|                     | GY                    | HUNNINGHAKE <i>et al.</i> Controlled trial of acifran in type II hyperlipoproteinemia. <i>Clinical pharmacology and therapeutics</i> (1985), 38(3), 313-7   |                |
|                     | GZ                    | SEKI <i>et al.</i> , Studies on hypolipidemic agents. II. Synthesis and pharmacological properties of alkylpyrazole derivatives. <i>Chemical &amp; Pharmaceutical Bulletin</i> (1984), 32(4), 1568-77   |                |
|                     | HA                    | VAN HERK <i>et al.</i> , Pyrazole Derivatives as Partial Agonists for the Nicotinic Acid Receptor. <i>Journal of Medicinal Chemistry</i> (2003), 46(18), 3945-3951  |                |
|                     | HB                    | MAHBOUBI <i>et al.</i> , Triglyceride modulation by acifran analogs: activity towards the niacin high and low affinity G protein-coupled receptors HM74A and HM74. <i>Biochemical and Biophysical Research Communications</i> (2006), 340(2), 482-490           |                |
|                     | HC                    | FROESCH <i>et al.</i> , Effects of 5-methylpyrazole-3-carboxylic acid on adipose tissue. II. Antilipolytic and hypoglycemic effects in vivo. <i>Molecular Pharmacol.</i> (1967), 3(5), 442-52   |                |
|                     | HD                    | Beilstein Records (BRN): 10958, Chemical Name (CN): 4-methyl-5-propionyl-1(2) <i>H</i> -pyrazole-3-carboxylic acid  |                |
|                     | HE                    | Beilstein Records (BRN): 14055, Chemical Name (CN): 4-methyl-5-propionyl-1(2) <i>H</i> -pyrazole-3-carboxylic acid ethyl ester  |                |

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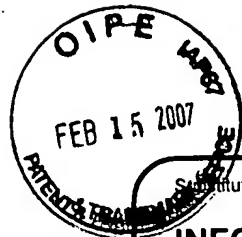
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Sheet 4 of 6

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|---------------------|-----------------------|---|----------------|
|                     | HF                    | GERRITSEN <i>et al.</i> , Effects of 5-methylpyrazole-3-carboxylic acid, U-19425, on FFA [free fatty acid] mobilization. <i>Advan. Exp. Med. Biol.</i> (1969), 4 93-103   |                |
|                     | HG                    | BIZZI <i>et al.</i> , Correlation between the effect of drugs on plasma free fatty acids and on tissue triglycerides. <i>Advan. Exp. Med. Biol.</i> (1969), 4 201-11  |                |
|                     | HH                    | GUNDERSEN <i>et al.</i> , Effects of 5-methylpyrazole-3-carboxylic and (U-19,425) and nicotinic acid (NA) on free fatty acids (FFA), triglycerides (TG), and cholesterol in man. <i>Advan. Exp. Med. Biol.</i> (1969), 4, 213-26                                |                |
|                     | HI                    | KIENER, Enzymic oxidation of methyl groups in heteroarenes: a versatile method for the preparation of heteroaromatic carboxylic acids. <i>Angew. Chem., Int. Ed. Engl.</i> , 1992, 31(6), 774-5   |                |
|                     | HJ                    | AKTORIES <i>et al.</i> , Inhibition of adenylate cyclase and stimulation of a high affinity GTPase by the antilipolytic agents, nicotinic acid, acipimox and various related compounds. <i>Arzneimittel-Forschung</i> (1983), 33(11), 1525-7                    |                |
|                     | HK                    | PRYOR <i>et al.</i> , Purification of maize alcohol dehydrogenase and competitive inhibition by pyrazoles. <i>Biochemistry International</i> (1982), 4(4), 431-8  |                |
|                     | HL                    | BIZZI <i>et al.</i> , Effects of antilipolytic agents on glucose utilization by adipose tissue. <i>Biochemical Pharmacology</i> (1973), 22(6), 763-8  |                |
|                     | HM                    | MYLES <i>et al.</i> , The development of tolerance to antilipolytic agents in rats. <i>Biochemical Pharmacology</i> (1985), 34(2), 269-74   |                |
|                     | HN                    | STRATTON <i>et al.</i> , The development of tolerance to antilipolytic agents by isolated rat adipocytes. <i>Biochemical Pharmacology</i> (1985), 34(2), 275-9  |                |
|                     | HO                    | COTTINEAU <i>et al.</i> , Synthesis and hypoglycemic evaluation of substituted pyrazole-4-carboxylic acids. <i>Bioorganic &amp; Medicinal Chemistry Letters</i> (2002), 12(16), 2105-2108   |                |
|                     | HP                    | HAMILTON <i>et al.</i> , The inhibition of mammalian D-amino acid oxidase by metabolites and drugs. Inferences concerning physiological function. <i>Bioorganic Chemistry</i> (1982), 11(3), 350-70   |                |
|                     | HQ                    | ISSEKUTZ, Effect of nicotinic acid, 5-methylpyrazole-3-carboxylic acid (U-19425), and dibutylrly cyclic AMP on renal gluconeogenesis. <i>Canadian Journal of Physiology and Pharmacology</i> (1971), 49(2), 102-5   |                |
|                     | HR                    | REIMLINGER <i>et al.</i> , Syntheses with silver or sodium pyrazoles. II. Reactions of the silver salts of methylpyrazoles with halogens. <i>Chemische Berichte</i> (1970), 103(6), 1949-53   |                |
|                     | HS                    | SEKIHACHI <i>et al.</i> , Synthesis and chromophoric properties of symmetrical bis-heteroannulated diketopiperazines: diimidazo- and dipyrazolo-piperazinediones. <i>Dyes and Pigments</i> (1996), 32(1), 43-58   |                |
|                     | HT                    | TIHANYI <i>et al.</i> , Pyrazolecarboxylic acid hydrazides as antiinflammatory agents. New selective lipoxygenase inhibitors. <i>European Journal of Medicinal Chemistry</i> (1984), 19(5), 433-9   |                |

|                    |  |                 |  |
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| Examiner Signature |  | Date Considered |  |
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|---------------------|-----------------------|---|----------------|
|                     | HU                    | BARALDI <i>et al.</i> , Synthesis, antibacterial activity and structure-activity relationships of N-substituted 4-diazopyrazole-5-carboxamides. 2. <i>Farmaco</i> (1991), 46(11), 1337-50   |                |
|                     | HV                    | ALBERTI <i>et al.</i> , Alkylpyrazoles. <i>Farmaco, Edizione Scientifica</i> (1961), 16 527-39  |                |
|                     | HW                    | ALEMAGNA <i>et al.</i> , Pyrazole synthesis from $\alpha$ -dicarbonyl compounds. <i>Gazzetta Chimica Italiana</i> (1963), 93(6), 748-56   |                |
|                     | HX                    | INFANTES <i>et al.</i> , Packing modes in eight 3-ethoxycarbonylpyrazole derivatives. Influence of the substituents on the crystal structure and annular tautomerism. <i>Heterocycles</i> (1999), 50(1), 227-242  |                |
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Sheet 6 of 6

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|                        |                     |
|------------------------|---------------------|
| Application Number     | 10/530,902          |
| Filing Date            | April 8, 2005       |
| First Named Inventor   | Graeme Semple       |
| Art Unit               | 1626                |
| Examiner Name          | Anderson, Rebecca L |
| Attorney Docket Number | 29.US2.PCT          |

**NON PATENT LITERATURE DOCUMENTS**

| Examiner Initials * | Cite No. <sup>1</sup> | Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published. | T <sup>2</sup> |
|---------------------|-----------------------|---|----------------|
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